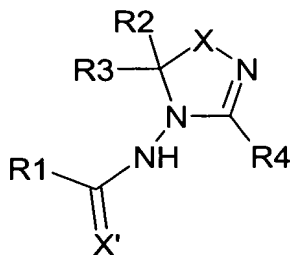


What is claimed is:

1. A compound of the general formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino;
- e) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, or (C₁-C₆)alkoxycarbonyl (-CO₂R^a);
- e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;

- f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, (C₁-C₄)alkoxycarbonyl (-CO₂R^a), or amino (-NR^aR^b);
- g) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or
- h) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino;

wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage (- (CH₂)_x-), an alkyloxyalkyl linkage (- (CH₂)_yO(CH₂)_z-), an alkylaminoalkyl linkage (- (CH₂)_yNR^a(CH₂)_z-), or an alkylbenzoalkyl linkage (- (CH₂)_y-1-benzo-2-(CH₂)_z-) form a ring with the carbon atom to which they are attached,

wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄)alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆)alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano (-OCH₂O-) or dioxano (-OCH₂CH₂O-) heterocyclic ring; wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

2. The compound of claim 1 wherein:

X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted benzothiophene-2-yl, or benzofuran-2-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, or (C₁-C₆)alkoxy;
- d) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;
- e) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, or (C₁-C₄)alkoxycarbonyl (-CO₂R^a);

f) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, or (C₁-C₆)alkyl; or

g) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, or (C₁-C₆)alkyl;

wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage $-(CH_2)_x-$, an alkyloxyalkyl linkage $-(CH_2)_yO(CH_2)_z-$, an alkylaminoalkyl linkage $-(CH_2)_yNR^a(CH_2)_z-$, or an alkylbenzoalkyl linkage $-(CH_2)_y-1-benzo-2-(CH_2)_z-$ form a ring with the carbon atom to which they are attached,

wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring; wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

3. The compound of claim 2 wherein:

X is O;

X' is O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, or (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)alkoxycarbonyl; carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); or phenyl; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted benzothiophene-2-yl, or benzofuran-2-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, or (C₁-C₆)alkoxy;
- d) unsubstituted or substituted furyl or thiophenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or phenyl;
- e) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, or (C₁-C₆)alkyl; or
- f) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, or (C₁-C₆)alkyl;

wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage (-(CH₂)_x-), an alkyloxyalkyl linkage (-(CH₂)_yO(CH₂)_z-), an alkylaminoalkyl linkage (-(CH₂)_yNR^a(CH₂)_z-), or an alkylbenzoalkyl linkage (-(CH₂)_y-1-benzo-2-(CH₂)_z-) form a ring with the carbon atom to which they are attached,

wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)alkoxycarbonyl; carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); or phenyl; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring; wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl; provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

4. The compound of claim 3 wherein:

X and X' are O;

R¹ is

phenyl, 4-chlorophenyl-, 4-ethylphenyl-, 2-ethyl-3,4-ethylenedioxyphenyl, 3-fluorophenyl-, 2-fluoro-4-ethylphenyl-, 2-methyl-3-methoxyphenyl-, 2-ethyl-3-methoxyphenyl, 3-methylphenyl-, 2-methoxyphenyl-, 2-nitrophenyl-, 3-nitrophenyl-, 2-furanyl-, benzyl-, benzothiophene-2-yl-, phenylamino-, benzyloxymethyl, phenoxymethyl-, 3-toluoylamino-, benzylamino-, benzoylamino-, ethoxycarbonylethyl-, or 3-chloro-2,2,3,3-tetrafluoroethyl;

R² and R³ are independently methyl, ethyl, or together as a tetramethylene $-(CH_2)_4-$, 4-pyrano $(-CH_2CH_2OCH_2CH_2-)$, or methylenebenzoethylene $(-CH_2-1-benzo-2-CH_2CH_2-)$ linkage form a ring with the carbon atom to which they are attached; and

R⁴ is phenyl, 4-biphenyl, 4-chlorophenyl, 2,4-dimethoxyphenyl, 3,5-dimethylphenyl, 2-methoxyphenyl, 3,4-methylenedioxyphenyl, 3-trifluoromethylphenyl, or 4-trifluoromethoxyphenyl;

provided that when R⁴ is phenyl, then R¹ is not phenyl.

5. The compound of claim 4 selected from the group consisting of:

1-Benzyl-3-[3-(3,5-dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-urea;

1-Benzoyl-3-[3-(3,5-dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-urea;

N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;

3-Chloro-N-[3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoropropionamide;

N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;

Benzo[b]thiophene-2-carboxylic acid [3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;

N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;

1-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;

N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;

2-Benzyloxy-N-[3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;
Furan-2-carboxylic acid [3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
Benzo[b]thiophene-2-carboxylic acid [5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
1-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-benzamide;
3-Chloro-N-[5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
1-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
2-Benzyloxy-N-[5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-acetamide;
Furan-2-carboxylic acid [5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
4-Ethyl-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
Benzo[b]thiophene-2-carboxylic acid [5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
3-Chloro-2,2,3,3-tetrafluoro-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-propionamide;

N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
2-Ethyl-3-methoxy-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid (3-benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-amide;
1-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-3-phenyl-urea;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-phenoxy-acetamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-benzyloxy-acetamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-phenyl-acetamide;
Furan-2-carboxylic acid (3-benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-amide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-ethyl-3-methoxy-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-(3-Biphenyl-4-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-benzamide;

N-(3-Biphenyl-4-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-ethyl-3-methoxy-benzamide;
4-Ethyl-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-benzamide;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-benzamide;
Benzo[b]thiophene-2-carboxylic acid (5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide;
1-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-3-phenyl-urea;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-2-phenoxy-acetamide;
2-Benzyloxy-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-acetamide;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-2-phenyl-acetamide;
Furan-2-carboxylic acid (5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide;
2-Ethyl-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-3-methoxy-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-benzamide;
3-Chloro-N-[3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
4-Ethyl-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
N-(3-Phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
3-Chloro-2,2,3,3-tetrafluoro-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-propionamide;
N-(3-Phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid (3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-amide;
1-Phenyl-3-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-urea;
2-Phenoxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;
2-Benzyloxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;

2-Phenyl-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;
Furan-2-carboxylic acid (3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-amide;
2-Ethyl-3-methoxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-benzamide;
3-Chloro-N-[3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-amide;
1-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-amide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-ethyl-3-methoxy-benzamide;
4-Ethyl-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
N-(3-Phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
1-Phenyl-3-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-urea;
2-Phenoxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Benzyloxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Phenyl-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Ethyl-3-methoxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-benzamide;
1-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-phenyl-acetamide;

Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1,8-dioxo-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-amide;
 N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxo-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-ethyl-3-methoxy-benzamide;
 N-[3-(3,5-Dimethyl-phenyl)-1-oxo-2,4-diaza-spiro[4.5]-7,8-benzo-dec-2-en-4-yl]-3-methoxy-2-methyl-benzamide;
 N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxo-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-3-methoxy-2-methyl-benzamide;
 N-[3-(3,5-Dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-methoxy-2-methyl-benzamide;
 N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-2-fluoro-benzamide;
 4-Ethyl-2-fluoro-N-(3-phenyl-1-oxo-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
 N-[3-(3,5-Dimethyl-phenyl)-1-oxo-2,4-diaza-spiro[4.4]non-2-en-4-yl]-4-ethyl-2-fluoro-benzamide;
 N-(5,5-Dimethyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-2-fluoro-benzamide;
 5-Ethyl-2,3-dihydro-benzo[1,4]dioxine-6-carboxylic acid (5,5-dimethyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide; and
 5-Ethyl-2,3-dihydro-benzo[1,4]dioxine-6-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide.

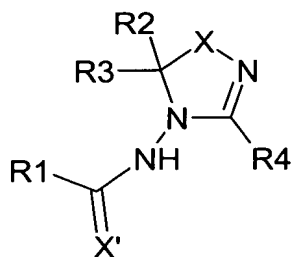
6. A method of modulating the expression of a target gene in a host cell, wherein the host cell includes a first gene expression cassette comprising a first polynucleotide encoding a first polypeptide comprising:

- (i) a transactivation domain;
- (ii) a DNA-binding domain; and
- (iii) a Group H nuclear receptor ligand binding domain;

a second gene expression cassette comprising:

- (i) a response element capable of binding to said DNA binding domain;
- (ii) a promoter that is activated by the transactivation domain; and
- (iii) said target gene;

the method comprising contacting said host cell with a compound of the formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino;
- f) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, or (C₁-C₆)alkoxycarbonyl (-CO₂R^a);
- e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;
- f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl,

(C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, (C₁-C₄)alkoxycarbonyl (-CO₂R^a), or amino (-NR^aR^b);

g) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or

h) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino;

wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage (-CH₂)_x-, an alkyloxylalkyl linkage (-CH₂)_yO(CH₂)_z-, an alkylaminoalkyl linkage (-CH₂)_yNR^a(CH₂)_z-, or an alkylbenzoalkyl linkage (-CH₂)_y-1-benzo-2-(CH₂)_z- form a ring with the carbon atom to which they are attached,

wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄)alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆)alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano (-OCH₂O-) or dioxano (-OCH₂CH₂O-) heterocyclic ring; wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

7. The method of claim 6 wherein the compound is of the specified formula and:

X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted benzothiophene-2-yl, or benzofuran-2-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, or (C₁-C₆)alkoxy;
- d) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;
- e) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, or (C₁-C₄)alkoxycarbonyl (-CO₂R^a);
- f) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, or (C₁-C₆)alkyl; or

g) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, or (C₁-C₆)alkyl;
wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage $-(CH_2)_x-$, an alkylloxylalkyl linkage $-(CH_2)_yO(CH_2)_z-$, an alkylaminoalkyl linkage $-(CH_2)_yNR^a(CH_2)_z-$, or an alkylbenzoalkyl linkage $-(CH_2)_y-1\text{-benzo-}2\text{-(CH}_2\text{)}_z-$ form a ring with the carbon atom to which they are attached,
wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)alkanoyloxy $(-OCOR^a)$; carboxamido $(-CONR^aR^b)$; amido $(-NR^aCOR^b)$; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido $(-S(O)R^a)$; sulfamido $(-SO_2NR^aR^b)$; or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage $(-OCH_2O-)$ or $(-OCH_2CH_2O-)$ to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring; wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

8. The method of Claim 7 wherein the compound is of the specified formula and:

X is O;

X' is O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, or (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)alkoxycarbonyl; carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); or phenyl; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted benzothiophene-2-yl, or benzofuran-2-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, or (C₁-C₆)alkoxy;
- d) unsubstituted or substituted furyl or thiophenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or phenyl;
- e) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, or (C₁-C₆)alkyl; or
- f) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, or (C₁-C₆)alkyl;

wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage (-(CH₂)_x-), an alkyloxyalkyl linkage (-(CH₂)_yO(CH₂)_z-), an alkylaminoalkyl linkage (-(CH₂)_yNR^a(CH₂)_z-), or an alkylbenzoalkyl linkage (-(CH₂)_y-1-benzo-2-(CH₂)_z-) form a ring with the carbon atom to which they are attached, wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)alkoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)alkoxycarbonyl; carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); or phenyl; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring; wherein R^a and R^b are independently H, (C₁-C₆)alkyl, or phenyl; provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and when R⁴ is phenyl, then R¹ is not phenyl, when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl.

9. The method of Claim 8 wherein the compound is of the specified formula and:

X and X' are O;

R¹ is

phenyl, 4-chlorophenyl-, 4-ethylphenyl-, 2-ethyl-3,4-ethylenedioxyphenyl, 3-fluorophenyl-, 2-fluoro-4-ethylphenyl-, 2-methyl-3-methoxyphenyl-, 2-ethyl-3-methoxyphenyl, 3-methylphenyl-, 2-methoxyphenyl-, 2-nitrophenyl-, 3-nitrophenyl-, 2-furanyl-, benzyl-, benzothiophene-2-yl-, phenylamino-, benzyloxymethyl, phenoxymethyl-, 3-toluoilamino-, benzylamino-, benzoylamino-, ethoxycarbonyl-, or 3-chloro-2,2,3,3-tetrafluoroethyl;

R² and R³ are independently methyl, ethyl, or together as a tetramethylene $-(CH_2)_4-$, 4-pyrano $-(CH_2CH_2OCH_2CH_2-)$, or methylenebenzoethylene $-(CH_2-1-benzo-2-CH_2CH_2-)$ linkage form a ring with the carbon atom to which they are attached; and

R⁴ is phenyl, 4-biphenyl, 4-chlorophenyl, 2,4-dimethoxyphenyl, 3,5-dimethylphenyl, 2-methoxyphenyl, 3,4-methylenedioxyphenyl, 3-trifluoromethylphenyl, or 4-trifluoromethoxyphenyl;

provided that when R⁴ is phenyl, then R¹ is not phenyl.

10. The method of claim 9, wherein the compound is selected from the group consisting of:

- 1-Benzyl-3-[3-(3,5-dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-urea;
- 1-Benzoyl-3-[3-(3,5-dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-urea;
- N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
- 3-Chloro-N-[3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoropropionamide;
- N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
- Benzo[b]thiophene-2-carboxylic acid [3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
- N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
- 1-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
- N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
- 2-Benzyloxy-N-[3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;

Furan-2-carboxylic acid [3-(4-chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
N-[3-(4-Chloro-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
Benzo[b]thiophene-2-carboxylic acid [5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
1-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [5,5-dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
N-[5,5-Dimethyl-3-(4-trifluoromethoxy-phenyl)-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-benzamide;
3-Chloro-N-[5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
1-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
2-Benzyloxy-N-[5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-acetamide;
Furan-2-carboxylic acid [5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
4-Ethyl-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
N-[5,5-Dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
Benzo[b]thiophene-2-carboxylic acid [5,5-dimethyl-3-(3-trifluoromethyl-phenyl)-[1,2,4]oxadiazol-4-yl]-amide;
3-Chloro-2,2,3,3-tetrafluoro-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-propionamide;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;

Benzo[b]thiophene-2-carboxylic acid [3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(2-Methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
2-Ethyl-3-methoxy-N-[3-(2-methoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-benzamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid (3-benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-amide;
1-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-3-phenyl-urea;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-phenoxy-acetamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-benzyloxy-acetamide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-phenyl-acetamide;
Furan-2-carboxylic acid (3-benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-amide;
N-(3-Benzo[1,3]dioxol-5-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-ethyl-3-methoxy-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-benzamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(2,4-dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(2,4-Dimethoxy-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
N-(3-Biphenyl-4-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-benzamide;
N-(3-Biphenyl-4-yl-5,5-dimethyl-[1,2,4]oxadiazol-4-yl)-2-ethyl-3-methoxy-benzamide;

4-Ethyl-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-benzamide;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-benzamide;
Benzo[b]thiophene-2-carboxylic acid (5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide;
1-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-3-phenyl-urea;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-2-phenoxy-acetamide;
2-Benzyloxy-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-acetamide;
N-(5-Ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-2-phenyl-acetamide;
Furan-2-carboxylic acid (5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide;
2-Ethyl-N-(5-ethyl-5-methyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-3-methoxy-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-benzamide;
3-Chloro-N-[3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide;
1-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide;
N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-2-ethyl-3-methoxy-benzamide;
4-Ethyl-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
N-(3-Phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
3-Chloro-2,2,3,3-tetrafluoro-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-propionamide;
N-(3-Phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid (3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-amide;
1-Phenyl-3-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-urea;
2-Phenoxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;
2-Benzyloxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;
2-Phenyl-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-acetamide;

Furan-2-carboxylic acid (3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-amide;
2-Ethyl-3-methoxy-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-benzamide;
3-Chloro-N-[3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2,2,3,3-tetrafluoro-propionamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-succinamic acid ethyl ester;
Benzo[b]thiophene-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-amide;
1-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-amide;
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-2-ethyl-3-methoxy-benzamide;
4-Ethyl-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
N-(3-Phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
1-Phenyl-3-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-urea;
2-Phenoxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Benzyloxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Phenyl-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-acetamide;
2-Ethyl-3-methoxy-N-(3-phenyl-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl)-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-4-ethyl-benzamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-benzamide;
1-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-3-phenyl-urea;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-phenoxy-acetamide;
2-Benzyloxy-N-[3-(3,5-dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-acetamide;
N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-phenyl-acetamide;
Furan-2-carboxylic acid [3-(3,5-dimethyl-phenyl)-1,8-dioxa-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-amide;

N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxo-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-2-ethyl-3-methoxy-benzamide;

N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.5]-7,8-benzo-dec-2-en-4-yl]-3-methoxy-2-methyl-benzamide;

N-[3-(3,5-Dimethyl-phenyl)-1,8-dioxo-2,4-diaza-spiro[4.5]dec-2-en-4-yl]-3-methoxy-2-methyl-benzamide;

N-[3-(3,5-Dimethyl-phenyl)-5,5-dimethyl-[1,2,4]oxadiazol-4-yl]-3-methoxy-2-methyl-benzamide;

N-[3-(3,5-Dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-4-ethyl-2-fluoro-benzamide;

4-Ethyl-2-fluoro-N-(3-phenyl-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl)-benzamide;

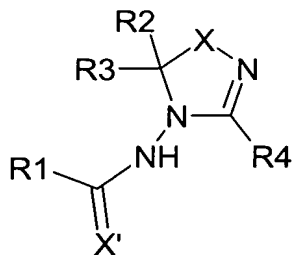
N-[3-(3,5-Dimethyl-phenyl)-1-oxa-2,4-diaza-spiro[4.4]non-2-en-4-yl]-4-ethyl-2-fluoro-benzamide;

N-(5,5-Dimethyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-4-ethyl-2-fluoro-benzamide;

5-Ethyl-2,3-dihydro-benzo[1,4]dioxine-6-carboxylic acid (5,5-dimethyl-3-phenyl-[1,2,4]oxadiazol-4-yl)-amide; and

5-Ethyl-2,3-dihydro-benzo[1,4]dioxine-6-carboxylic acid [3-(3,5-dimethyl-phenyl)-5-ethyl-5-methyl-[1,2,4]oxadiazol-4-yl]-amide.

11. A method to modulate the expression of one or more exogenous genes in a subject, comprising administering to the subject an effective amount of a ligand of the formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-

C_6)alkoxy(C_1 - C_6)alkoxy; (C_1 - C_6)alkanoyloxy(C_1 - C_6)alkyl; (C_2 - C_6)alkenyl optionally substituted with halo, cyano, (C_1 - C_4) alkyl, or (C_1 - C_4)alkoxy; (C_2 - C_6)alkynyl optionally substituted with halo or (C_1 - C_4)alkyl; formyl; carboxy; (C_1 - C_6)alkylcarbonyl; (C_1 - C_6)haloalkylcarbonyl; benzoyl; (C_1 - C_6)alkoxycarbonyl; (C_1 - C_6)haloalkoxycarbonyl; (C_1 - C_6)alkanoyloxy ($-OCOR^a$); carboxamido ($-CONR^aR^b$); amido ($-NR^aCOR^b$); alkoxycarbonylamino ($-NR^aCO_2R^b$); alkylaminocarbonylamino ($-NR^aCONR^bR^c$); mercapto; (C_1 - C_6)alkylthio; (C_1 - C_6) alkylsulfonyl; (C_1 - C_6)alkylsulfoxido ($-S(O)R^a$); sulfamido ($-SO_2NR^aR^b$); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1 - C_6) alkoxy, (C_1 - C_6)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage ($-OCH_2O-$) or ($-OCH_2CH_2O-$) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;

c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1 - C_6) alkoxy, (C_1 - C_6)alkyl, or amino;

d) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, carboxy, or (C_1 - C_6)alkoxycarbonyl ($-CO_2R^a$);

e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, or (C_1 - C_6)haloalkoxy;

f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, carboxy, (C_1 - C_6)alkoxycarbonyl ($-CO_2R^a$), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1 - C_6)alkyl, (C_1 - C_6)haloalkyl, (C_1 - C_6)alkoxy, (C_1 - C_6)haloalkoxy, carboxy, (C_1 - C_4)alkoxycarbonyl ($-CO_2R^a$), or amino ($-NR^aR^b$);

g) aromatic-substituted or unsubstituted phenyl(C_1 - C_6)alkyl, phenyl(C_1 - C_6)alkoxy(C_1 - C_6)alkyl, or phenoxy(C_1 - C_6)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C_1 - C_6) alkoxy, (C_1 - C_6)alkyl, or amino; or

h) aromatic-substituted or unsubstituted phenylamino, phenyl(C_1 - C_6)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C_1 - C_6) alkoxy, (C_1 - C_6)alkyl, or amino;

wherein R^a , R^b , and R^c are independently H, (C_1 - C_6)alkyl, or phenyl;

R^2 and R^3 are independently H, (C_1 - C_6)alkyl, (C_1 - C_6)haloalkyl, (C_1 - C_6)cyanoalkyl, (C_1 - C_6)hydroxyalkyl, (C_1 - C_6)alkoxy(C_1 - C_6)alkyl, phenyl, or together as an alkane linkage ($-(CH_2)_x-$), an alkyloxyalkyl linkage ($-(CH_2)_yO(CH_2)_z-$), an alkylaminoalkyl linkage ($-(CH_2)_yNR^a(CH_2)_z-$), or an alkylbenzoalkyl linkage ($-(CH_2)_y-1$ -benzo-2- $(CH_2)_z-$) form a ring with the carbon atom to which they are attached,

wherein $x = 3$ to 7 , $y = 1$ to 3 , $z = 1$ to 3 , and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R^4 is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano (-OCH₂O-) or dioxano (-OCH₂CH₂O-) heterocyclic ring; wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

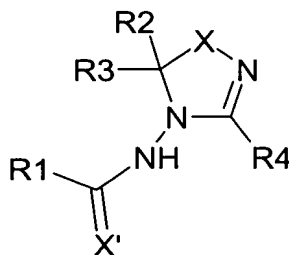
provided that R^4 is not 3-nitrophenyl or 4-nitrophenyl, and

when R^4 is phenyl, then R¹ is not phenyl,

when R^4 is 3-chlorophenyl, then R¹ is not phenylamino, or

when R^4 is 4-chlorophenyl, then R¹ is not methyl.

12. A method for regulating endogenous or heterologous gene expression in a transgenic subject comprising contacting a ligand with an ecdysone receptor complex within the cells of the subject, wherein the cells further contain a DNA binding sequence for the ecdysone receptor complex when in combination with the ligand and wherein formation of an ecdysone receptor complex-ligand-DNA binding sequence complex induces expression of the gene, and where the ligand has the following formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino;
- g) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, or (C₁-C₆)alkoxycarbonyl (-CO₂R^a);
- e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;
- f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, (C₁-C₄)alkoxycarbonyl (-CO₂R^a), or amino (-NR^aR^b);
- g) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or
- h) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino;

wherein R^a , R^b , and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

R^2 and R^3 are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage $-(CH_2)_x-$, an alkyloxylalkyl linkage $-(CH_2)_yO(CH_2)_z-$, an alkylaminoalkyl linkage $-(CH_2)_yNR^a(CH_2)_z-$, or an alkylbenzoalkyl linkage $-(CH_2)_y-1\text{-benzo-}2\text{-(CH}_2)_z-$ form a ring with the carbon atom to which they are attached,

wherein $x = 3$ to 7 , $y = 1$ to 3 , $z = 1$ to 3 , and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R^4 is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino ($-NR^aR^b$); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy ($-OCOR^a$); carboxamido ($-CONR^aR^b$); amido ($-NR^aCOR^b$); alkoxycarbonylamino ($-NR^aCO_2R^b$); alkylaminocarbonylamino ($-NR^aCONR^bR^c$); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido ($-S(O)R^a$); sulfamido ($-SO_2NR^aR^b$); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano ($-OCH_2O-$) or dioxano ($-OCH_2CH_2O-$) heterocyclic ring; wherein R^a , R^b , and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R^4 is not 3-nitrophenyl or 4-nitrophenyl, and

when R^4 is phenyl, then R^1 is not phenyl,

when R^4 is 3-chlorophenyl, then R^1 is not phenylamino, or

when R^4 is 4-chlorophenyl, then R^1 is not methyl.

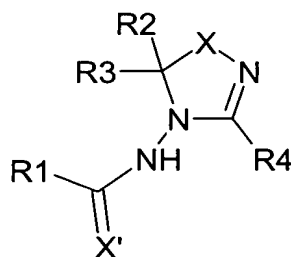
13. The method of Claim 12, wherein the ecdysone receptor complex is a chimeric ecdysone receptor complex and the DNA construct further comprises a promoter.

14. The method of Claim 12, wherein the subject is a plant.

15. The method of Claim 12, wherein the subject is a mammal.

16. A method of modulating the expression of a gene in a host cell comprising the steps of:

- a) introducing into the host cell a gene expression modulation system comprising:
 - i) a first gene expression cassette that is capable of being expressed in a host cell comprising a polynucleotide sequence that encodes a first hybrid polypeptide comprising:
 - (a) a DNA-binding domain that recognizes a response element associated with a gene whose expression is to be modulated; and
 - (b) an ecdysone receptor ligand binding domain;
 - ii) a second gene expression cassette that is capable of being expressed in the host cell comprising a polynucleotide sequence that encodes a second hybrid polypeptide comprising:
 - (a) a transactivation domain; and
 - (b) a chimeric retinoid X receptor ligand binding domain; and
 - iii) a third gene expression cassette that is capable of being expressed in a host cell comprising a polynucleotide sequence comprising:
 - (a) a response element recognized by the DNA-binding domain of the first hybrid polypeptide;
 - (b) a promoter that is activated by the transactivation domain of the second hybrid polypeptide; and
 - (c) a gene whose expression is to be modulated; and
- b) introducing into the host cell a ligand of the formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-

C_6)cyanoalkyl; (C_1-C_6) hydroxyalkyl; (C_1-C_6) alkoxy; phenoxy; (C_1-C_6) haloalkoxy; (C_1-C_6) alkoxy (C_1-C_6) alkyl; (C_1-C_6) alkoxy (C_1-C_6) alkoxy; (C_1-C_6) alkanoyloxy (C_1-C_6) alkyl; (C_2-C_6) alkenyl optionally substituted with halo, cyano, (C_1-C_4) alkyl, or (C_1-C_4) alkoxy; (C_2-C_6) alkynyl optionally substituted with halo or (C_1-C_4) alkyl; formyl; carboxy; (C_1-C_6) alkylcarbonyl; (C_1-C_6) haloalkylcarbonyl; benzoyl; (C_1-C_6) alkoxycarbonyl; (C_1-C_6) haloalkoxycarbonyl; (C_1-C_6) alkanoyloxy $(-OCOR^a)$; carboxamido $(-CONR^aR^b)$; amido $(-NR^aCOR^b)$; alkoxycarbonylamino $(-NR^aCO_2R^b)$; alkylaminocarbonylamino $(-NR^aCONR^bR^c)$; mercapto; (C_1-C_6) alkylthio; (C_1-C_6) alkylsulfonyl; (C_1-C_6) alkylsulfoxido $(-S(O)R^a)$; sulfamido $(-SO_2NR^aR^b)$; or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1-C_6) alkoxy, (C_1-C_6) alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage $(-OCH_2O-)$ or $(-OCH_2CH_2O-)$ to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;

c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1-C_6) alkoxy, (C_1-C_6) alkyl, or amino;

d) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, carboxy, or (C_1-C_6) alkoxycarbonyl $(-CO_2R^a)$;

e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, or (C_1-C_6) haloalkoxy;

f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, carboxy, (C_1-C_6) alkoxycarbonyl $(-CO_2R^a)$, or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C_1-C_6) alkyl, (C_1-C_6) haloalkyl, (C_1-C_6) alkoxy, (C_1-C_6) haloalkoxy, carboxy, (C_1-C_4) alkoxycarbonyl $(-CO_2R^a)$, or amino $(-NR^aR^b)$;

g) aromatic-substituted or unsubstituted phenyl (C_1-C_6) alkyl, phenyl (C_1-C_6) alkoxy (C_1-C_6) alkyl, or phenoxy (C_1-C_6) alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C_1-C_6) alkoxy, (C_1-C_6) alkyl, or amino; or

h) aromatic-substituted or unsubstituted phenylamino, phenyl (C_1-C_6) alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C_1-C_6) alkoxy, (C_1-C_6) alkyl, or amino;

wherein R^a , R^b , and R^c are independently H, (C_1-C_6) alkyl, or phenyl;

R^2 and R^3 are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage $-(CH_2)_x-$, an alkyloxylalkyl linkage $-(CH_2)_yO(CH_2)_z-$, an alkylaminoalkyl linkage $-(CH_2)_yNR^a(CH_2)_z-$, or an alkylbenzoalkyl linkage $-(CH_2)_y-1-benzo-2-(CH_2)_z-$ form a ring with the carbon atom to which they are attached,

wherein $x = 3$ to 7 , $y = 1$ to 3 , $z = 1$ to 3 , and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R^4 is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino ($-NR^aR^b$); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy ($-OCOR^a$); carboxamido ($-CONR^aR^b$); amido ($-NR^aCOR^b$); alkoxycarbonylamino ($-NR^aCO_2R^b$); alkylaminocarbonylamino ($-NR^aCONR^bR^c$); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido ($-S(O)R^a$); sulfamido ($-SO_2NR^aR^b$); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano ($-OCH_2O-$) or dioxano ($-OCH_2CH_2O-$) heterocyclic ring; wherein R^a , R^b , and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R^4 is not 3-nitrophenyl or 4-nitrophenyl, and

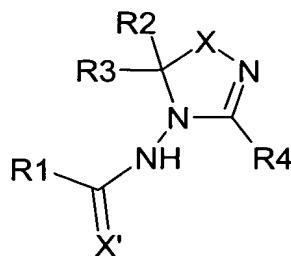
when R^4 is phenyl, then R^1 is not phenyl,

when R^4 is 3-chlorophenyl, then R^1 is not phenylamino, or

when R^4 is 4-chlorophenyl, then R^1 is not methyl.

17. A method for producing a polypeptide comprising the steps of:

- a) selecting a cell which is substantially insensitive to exposure to a ligand comprising the formula:



wherein X and X' are independently O or S;

R¹ is

- a) H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, or benzyloxy;
- b) unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄) alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆) alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined as a linkage (-OCH₂O-) or (-OCH₂CH₂O-) to form a 5- or 6-membered dioxolano or dioxano heterocyclic ring;
- c) unsubstituted or substituted naphthyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆) alkoxy, (C₁-C₆)alkyl, or amino;
- d) unsubstituted or substituted benzothiophene-2-yl, benzothiophene-3-yl, benzofuran-2-yl, or benzofuran-3-yl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, or (C₁-C₆)alkoxycarbonyl (-CO₂R^a);
- e) unsubstituted or substituted 2, 3, or 4-pyridyl wherein the substituents are independently 1 to 3 halo, cyano, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkoxy;
- f) unsubstituted or substituted 5-membered heterocycle selected from furyl, thiophenyl, triazolyl, pyrrolyl, isopyrrolyl, pyrazolyl, isoimidazolyl, thiazolyl, isothiazolyl, oxazolyl, or isooxazolyl wherein the substituents are independently 1 to 3 halo, nitro, hydroxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, carboxy, (C₁-C₆)alkoxycarbonyl (-CO₂R^a), or unsubstituted or substituted phenyl wherein the substituents are

independently 1 to 3 halo, nitro, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)alkoxy, (C₁-C₆)haloalkoxy, carboxy, (C₁-C₄)alkoxycarbonyl (-CO₂R^a), or amino (-NR^aR^b);

g) aromatic-substituted or unsubstituted phenyl(C₁-C₆)alkyl, phenyl(C₁-C₆)alkoxy(C₁-C₆)alkyl, or phenoxy(C₁-C₆)alkyl wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or

h) aromatic-substituted or unsubstituted phenylamino, phenyl(C₁-C₆)alkylamino, or phenylcarbonylamino wherein the aromatic substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino;

wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

R² and R³ are independently H, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, (C₁-C₆)cyanoalkyl, (C₁-C₆)hydroxyalkyl, (C₁-C₆)alkoxy(C₁-C₆)alkyl, phenyl, or together as an alkane linkage (- (CH₂)_x-), an alkyloxylalkyl linkage (- (CH₂)_yO(CH₂)_z-), an alkylaminoalkyl linkage (- (CH₂)_yNR^a(CH₂)_z-), or an alkylbenzoalkyl linkage (- (CH₂)_y-1-benzo-2-(CH₂)_z-) form a ring with the carbon atom to which they are attached,

wherein x = 3 to 7, y = 1 to 3, z = 1 to 3, and R^a is H, (C₁-C₆)alkyl, or phenyl; and

R⁴ is unsubstituted or substituted phenyl wherein the substituents are independently 1 to 5 H; halo; nitro; cyano; hydroxy; amino (-NR^aR^b); (C₁-C₆)alkyl; (C₁-C₆)haloalkyl; (C₁-C₆)cyanoalkyl; (C₁-C₆)hydroxyalkyl; (C₁-C₆)alkoxy; phenoxy; (C₁-C₆)haloalkoxy; (C₁-C₆)alkoxy(C₁-C₆)alkyl; (C₁-C₆)alkoxy(C₁-C₆)alkoxy; (C₁-C₆)alkanoyloxy(C₁-C₆)alkyl; (C₂-C₆)alkenyl optionally substituted with halo, cyano, (C₁-C₄)alkyl, or (C₁-C₄)alkoxy; (C₂-C₆)alkynyl optionally substituted with halo or (C₁-C₄)alkyl; formyl; carboxy; (C₁-C₆)alkylcarbonyl; (C₁-C₆)haloalkylcarbonyl; benzoyl; (C₁-C₆)alkoxycarbonyl; (C₁-C₆)haloalkoxycarbonyl; (C₁-C₆)alkanoyloxy (-OCOR^a); carboxamido (-CONR^aR^b); amido (-NR^aCOR^b); alkoxycarbonylamino (-NR^aCO₂R^b); alkylaminocarbonylamino (-NR^aCONR^bR^c); mercapto; (C₁-C₆)alkylthio; (C₁-C₆)alkylsulfonyl; (C₁-C₆)alkylsulfoxido (-S(O)R^a); sulfamido (-SO₂NR^aR^b); or unsubstituted or substituted phenyl wherein the substituents are independently 1 to 3 halo, nitro, (C₁-C₆)alkoxy, (C₁-C₆)alkyl, or amino; or when two adjacent positions on the phenyl ring are substituted with alkoxy groups, these groups, together with the carbon atoms to which they are attached, may be joined to form a 5- or 6-membered dioxolano (-OCH₂O-) or dioxano (-OCH₂CH₂O-) heterocyclic ring; wherein R^a, R^b, and R^c are independently H, (C₁-C₆)alkyl, or phenyl;

provided that R⁴ is not 3-nitrophenyl or 4-nitrophenyl, and

when R⁴ is phenyl, then R¹ is not phenyl,

when R⁴ is 3-chlorophenyl, then R¹ is not phenylamino, or

when R⁴ is 4-chlorophenyl, then R¹ is not methyl;

b) introducing into the cell:

1) a DNA construct comprising:

- i) an exogenous gene encoding the polypeptide; and
- ii) a response element;

wherein the gene is under the control of the response element; and

2) an ecdysone receptor complex comprising:

- i) a DNA binding domain;
- ii) a binding domain for the ligand; and
- iii) a transactivation domain; and

c) exposing the cell to the ligand.